Comparative Efficacy of Intralesional Injections for the Treatment of Hypertrophic Scars

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Abstract

Facial Hypertrophic scars are clinically relevant as they can produce decreased self-esteem, lower self-confidence, and increase anxiety, decreasing the quality of life of patients. It is estimated that $4 billion are spent annually for the treatment of scars in the United States. Hypertrophic scar formation is characterized by dysregulation of the wound healing process by inflammation and fibrosis. Medications for hypertrophic scars have been studied and implemented, such as 5-FU, dexamethasone, and triamcinolone, but there are no studies that compare the efficacy of each of these treatments as well as the efficacy of combined treatments. Using a reproducible rabbit ear model, the efficacy of treatments for hypertrophic scars can be elucidated. 4-6 wounds are produced in each of the animal's ear. These wounds are monitored over 30 days until they mature into a developed hypertrophic scar. Single and combination treatments of dexamethasone, triamcolone acetate, 5-Florouracil or saline are injected into the individual scar. Two more doses of medications are administered to the scar after 3 weeks and 6 weeks after the first treatment. After 9 weeks since the first injection, gross images are taken, and the animals are euthanized for tissue collection and histopathological assessment of the scar depth and height to evaluate and compare the efficacy of the different treatments in a qualitative and quantitative fashion. The models are compared to each other as well as to the control group. With this study, the optimal intralesional treatment for hypertrophic scars can be evaluated. Results from this experiment will lead to greater reliability of scar healing treatments, practitioner consistency in the treatment of hypertrophic scars, decreased costs through targeted care, and improved cosmetic outcomes that enhance patients' quality of life.

Introduction

Despite recent advances in the number of substances that have demonstrated efficacy in treating hypertrophic scars, a standard, clinically optimized treatment protocol has yet to be established. Of the injectable medications available, triamcinolone is among the most heavily investigated and widely used clinically. However, inconsistent success rates and adverse outcomes including pain, atrophy and hypopigmentation at the site of injection warrants investigation of alternatives (Khalid et. al. 2019). Furthermore, case reports of subcutaneous triamcinolone injection of the face demonstrate a very rare incidence of microemboli resulting in retinal arteriole occlusion (Li et. al. 2018). In this study, we utilized a standardized, well-described animal model to rigorously compare the efficacy of triamcinolone to dexamethasone, an aqueous steroid alternative, as well as the antimetabolite 5-fluorouracil.

Methods

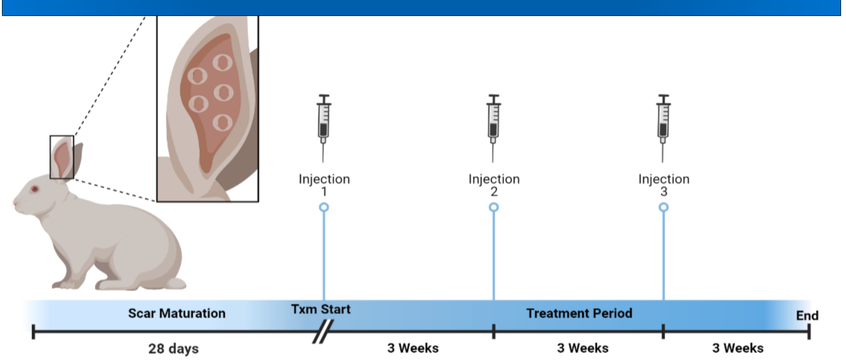

Figure 1: Rabbit ear hypertrophic scar model and treatment time course. 5 wounds were created per ear using standard method described by Kloesters et. al. 2007. Wounds matured into scars over 28 days when they are fully epithelialized. Each scar underwent 3 rounds of treatment with 1 of 5 injections (saline, dexamethasone, triamcinolone, 5-FU, dex+5-FU) in each ear every 3 weeks. Rabbits are sacrificed 3 weeks after the final injection and scars are collected for histologic analysis and molecular analysis.

Results

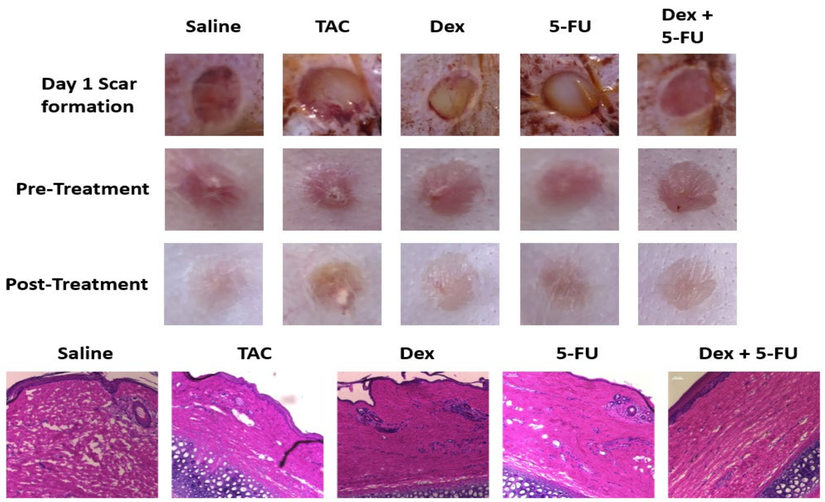

Figure 2: Gross images of POD1, POD28 (pre-treatment) and final post-treatment scars after 3 rounds of treatment (a) with representative 100x microscopic images of scars post-treatment (b). Slides were stained with hematoxylin and eosin TAC = triamcinolone; Dex = dexamethasone; 5-FU = 5-Fluorouracil

Results (cont.)

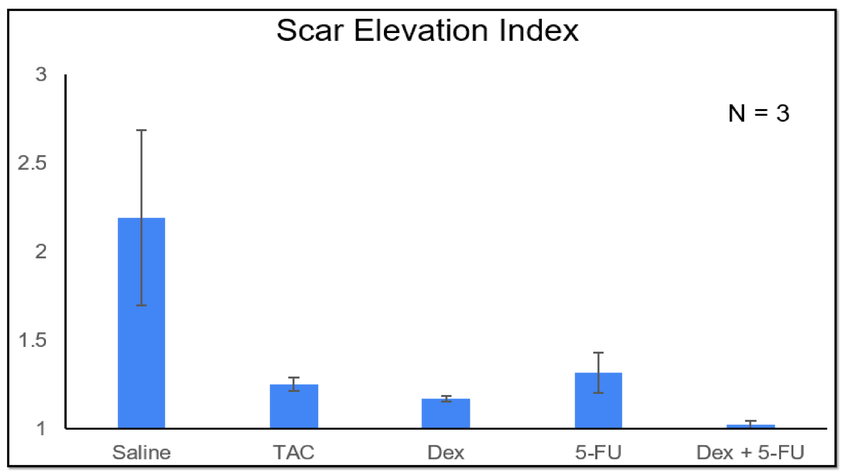

Figure 3: Influence of intralesional injections on scar elevation. Scar elevation index (SEI) was measured histologically using the ratio of the hypertrophied neodermis to the dermal thickness of normal adjacent skin. Error bars represent standard error of the mean.

Results (cont.)

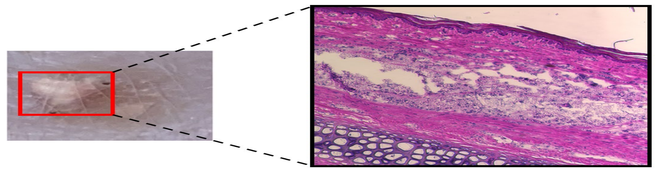

Figure 4: Presence of TAC precipitate present on both gross examination at experimental endpoint and on histologic examination.

Conclusion

- All treatment modalities demonstrate a trend towards reduced scar elevation after 3 rounds of treatment with combination Dex + 5-FU demonstrating the largest reduction in scar elevation
- TAC particulate can be present up to 3 weeks after injection in the dermis and impact the appearance. Dexamethasone provides similar elevation results without depositing particulates into the skin
- Further studies require increasing sample size to achieve statistical power and follow-up molecular analysis to provide mechanistic insight to each treatment's impact

References

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